

PTO/SB/17 (12-04v2)  
Approved for use through 7/31/2008. OMB 0851-0032  
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no person are required to respond to a collection of information unless it displays a valid OMB control number.

Effective on 12/08/2004.  
Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

## FEE TRANSMITTAL

### For FY 2005

☒ Applicant claims small entity status. See 37 CFR 1.27

<b>TOTAL AMOUNT OF PAYMENT</b>		(\$)		250.00	
--------------------------------	--	------	--	--------	--

**Complete if Known**

Application Number	10/049,504-Conf. #7626
Filing Date	June 18, 2002
First Named Inventor	Subramaniam Ananthan
Examiner Name	P. L. Morris
Art Unit	1625
Attorney Docket No.	21381-00053-US

**METHOD OF PAYMENT** (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ Note ☐ Other (please identify): \_\_\_\_\_

☒ Deposit Account Deposit Account Number: 22-0185 Deposit Account Name: Connolly Bove Lodge & Hutz LLP

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, except for the filing fee

☒ Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17 ☒ Credit any overpayments

**FEE CALCULATION**

**1. BASIC FILING, SEARCH, AND EXAMINATION FEES**

Application Type	FILING FEES		SEARCH FEES		EXAMINATION FEES		Fees Paid (\$)
	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	Fee (\$)	Small Entity Fee (\$)	
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

**2. EXCESS CLAIM FEES**

Fee Description	Fee (\$)	Small Entity Fee (\$)
Each claim over 20 (including Reissues)	50	25
Each independent claim over 3 (including Reissues)	200	100
Multiple dependent claims	360	180

**Total Claims**      **Extra Claims**      **Fee (\$)**      **Fee Paid (\$)**      **Multiple Dependent Claims**

\_\_\_\_\_ - 20 = \_\_\_\_\_ x \_\_\_\_\_ = \_\_\_\_\_      **Fee (\$)**      **Fee Paid (\$)**

**Indep. Claims**      **Extra Claims**      **Fee (\$)**      **Fee Paid (\$)**

\_\_\_\_\_ - 3 = \_\_\_\_\_ x \_\_\_\_\_ = \_\_\_\_\_

**3. APPLICATION SIZE FEE**

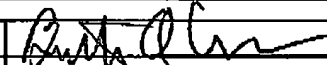
If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(e).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee (\$)	Fee Paid (\$)
_____	_____	_____ / 50 (round up to a whole number) x	_____	_____

**4. OTHER FEE(S)**

	Fee Paid (\$)
Non-English Specification, \$130 fee (no small entity discount)	
Other (e.g., late filing surcharge): 2402 Filing a brief in support of an appeal	250.00

**SUBMITTED BY**

Signature		Registration No. (Attorney/Agent)	24,852	Telephone	(202) 331-7111
Name (Print/Type)	Burton A. Americk	Date	5-25-05		

 RECEIVED  
 MAY 26 2005  
 OIPE/JCWS

MAY 25 2005

**FAX TRANSMISSION**DATE: May 25, 2005PTO IDENTIFIER: Application Number 10/049,504-Conf. #7626  
Patent Number

Inventor: Subramaniam Ananthan

MESSAGE TO: US Patent and Trademark Office

FAX NUMBER: (703) 872-9306

FROM: CONNOLLY BOVE LODGE &amp; HUTZ LLP

Burton A. Amernick

PHONE: (202) 331-7111

Attorney Dkt. #: 21381-00053-US

PAGES (Including Cover Sheet): 16

CONTENTS: Fee Transmittal (1 page)  
Appeal Brief Transmittal (1 page)  
Appeal Brief (12 pages)  
Charge \$250.00 to deposit account 22-0185  
Certificate of Transmission (1 page)

If your receipt of this transmission is in error, please notify this firm immediately by collect call to sender at (202) 331-7111 and send the original transmission to us by return mail at the address below.

This transmission is intended for the sole use of the individual and entity to whom it is addressed, and may contain information that is privileged, confidential and exempt from disclosure under applicable law. You are hereby notified that any dissemination, distribution or duplication of this transmission by someone other than the intended addressee or its designated agent is strictly prohibited.

CONNOLLY BOVE LODGE & HUTZ LLP  
1990 M Street, N.W., Suite 800, Washington, DC 20036-3425  
Telephone: (202) 331-7111 Facsimile: (202) 293-6229

PTO/SB/97 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031

U. S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Application No. (if known): 10/049,504

Attorney Docket No.: 21381-00053-US

**Certificate of Transmission under 37 CFR 1.8**

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office.

on May 25, 2005  
Date

Nicole Brown  
Signature

Nicole Brown

Typed or printed name of person signing Certificate

Registration Number, if applicable

(202) 331-7111

Telephone Number

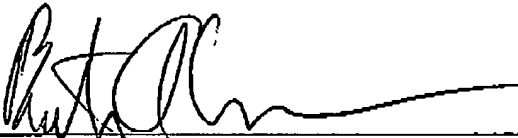
Note: Each paper must have its own certificate of transmission, or this certificate must identify each submitted paper.

Fee Transmittal (1 page)

Appeal Brief Transmittal (1 page)

Appeal Brief (12 pages)

Charge \$250.00 to deposit account 22-0185

TRANSMITTAL OF APPEAL BRIEF			Docket No. 21381-00053-US
In re Application of: Subramaniam Ananthan			
Application No. 10/049,504-Conf. #7626	Filing Date June 18, 2002	Examiner P. L. Morris	Group Art Unit 1625
Invention: PYRIDOMORPHINANS, THIENOMORPHINANS AND USE THEREOF			
<b><u>TO THE COMMISSIONER OF PATENTS:</u></b>			
Transmitted herewith is the Appeal Brief in this application, with respect to the Notice of Appeal filed: <u>April 8, 2005</u> .			
The fee for filing this Appeal Brief is <u>\$ 250.00</u> .			
<input type="checkbox"/> Large Entity <input checked="" type="checkbox"/> Small Entity			
<input type="checkbox"/> A petition for extension of time is also enclosed.			
The fee for the extension of time is _____.			
<input type="checkbox"/> A check in the amount of _____ is enclosed.			
<input checked="" type="checkbox"/> Charge the amount of the fee to Deposit Account No. <u>22-0185</u> . This sheet is submitted in duplicate.			
<input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.			
<input checked="" type="checkbox"/> The Director is hereby authorized to charge any additional fees that may be required or credit any overpayment to Deposit Account No. <u>22-0185</u> . This sheet is submitted in duplicate.			
		Dated: <u>5-25-05</u>	
Burton A. Amernick Attorney Reg. No. : 24,852 CONNOLLY BOVE LODGE & HUTZ LLP 1990 M Street, N.W., Suite 800 Washington, DC 20036-3425 (202) 331-7111			

RECEIVED  
CENTRAL FAX CENTER

MAY 25 2005

Docket No.: 21381-00053-US  
(PATENT)

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

---

In re Patent Application of:  
Subramaniam Ananthan

Application No.: 10/049,504

Confirmation No.: 7626

Filed: June 18, 2002

Art Unit: 1625

For: PYRIDOMORPHINANS,  
THIENOMORPHINANS AND USE THEREOF

Examiner: P. L. Morris

**APPEAL BRIEF**MS Appeal Brief - Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

As required under § 41.37(a), this brief is filed within two months of the Notice of Appeal filed in this case on April 8, 2005, and is in furtherance of said Notice of Appeal.

The fees required under § 41.20(b)(2) are dealt with in the accompanying  
TRANSMITTAL OF APPEAL BRIEF.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37  
and M.P.E.P. § 1206:

- |       |                                               |
|-------|-----------------------------------------------|
| I.    | Real Party In Interest                        |
| II    | Related Appeals and Interferences             |
| III.  | Status of Claims                              |
| IV.   | Status of Amendments                          |
| V.    | Summary of Claimed Subject Matter             |
| VI.   | Grounds of Rejection to be Reviewed on Appeal |
| VII.  | Argument                                      |
| VIII. | Claims                                        |

394459

Application No.: 10/049,504

Docket No.: 21381-00053-US

IX. Evidence  
X. Related Proceedings  
Appendix A Claims

**I. REAL PARTY IN INTEREST**

The real party in interest for this appeal is:

Southern Research Institute

**II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS**

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

**III. STATUS OF CLAIMS**

**A. Total Number of Claims in Application**

There are 16 claims pending in application.

**B. Current Status of Claims**

1. Claims canceled: 0
2. Claims withdrawn from consideration but not canceled: 2-6 and 12-16
3. Claims pending: 1-16
4. Claims allowed: 0
5. Claims rejected: 1 and 7-11

**C. Claims on Appeal**

The claims on appeal are claims 1 and 7-11.

Application No.: 10/049,504

Docket No.: 21381-00053-US

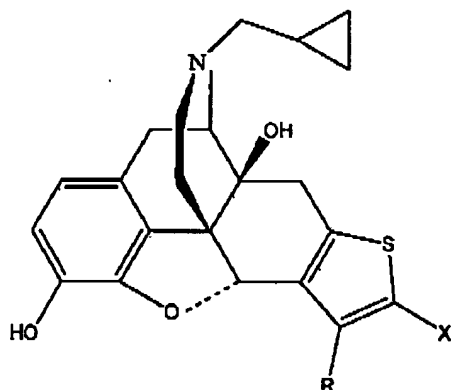
## IV. STATUS OF AMENDMENTS

Applicant filed an Amendment After Final Rejection on February 23, 2005. The Examiner responded to the Amendment After Final Rejection in an Advisory Action mailed March 10, 2005. In the Advisory Action, the Examiner indicated that Applicants' proposed amendments to claims 1 and 8 would not be entered.

Accordingly, the claims enclosed herein as Appendix A do not incorporate the amendments to claims 1 and 8, as indicated in the paper filed. However, the claims in Appendix A do incorporate the amendments indicated in the paper filed by Applicant on April 15, 2003.

## V. SUMMARY OF CLAIMED SUBJECT MATTER

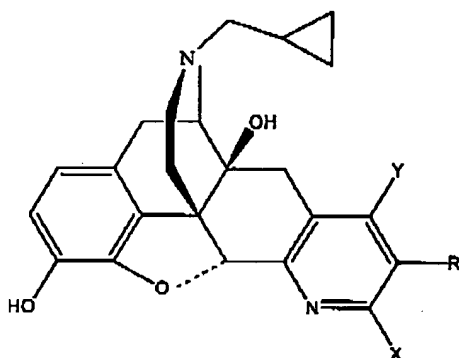
The claims on appeal relate to thienomorphinans represented by the formula:



wherein each of Y, X and R individually is selected from the group consisting of hydrogen, hydroxyl, halo, CF<sub>3</sub>, NO<sub>2</sub>, CN, NH<sub>2</sub>, COR<sup>1</sup> and CO<sub>2</sub>R<sup>2</sup> wherein R<sup>1</sup> is selected from the group consisting of alkyl, aryl, alkaryl, and NH<sub>2</sub>, and R<sup>2</sup> is selected from the group consisting of alkyl, aryl, and aralkyl, and provided that at least one of X and R in formula I is other than hydrogen; or pharmaceutically acceptable salt thereof (See page 3, line 14 to page 4, line 4 of the specification). Please note that claim 1 also still recites the non-elected compounds represented by the formula:

Application No.: 10/049,504

Docket No.: 21381-00053-US



However, the amendment filed after the final rejection on February 23, 2005, which the Examiner refused to enter, merely deleted this non-elected formula from the claim 1 and corrected a typographical error in claim 8 to change "2" to "II". Applicant hereby proffers to amend the claims in this manner if the Board wishes us to do so.

Compounds of the present invention exhibit high antagonistic activity at the  $\delta$  receptor (See page 1, lines 15 to 17 of the specification). Also as evidenced by compounds 8a-8f in Table 3 on page 22 of the specification, *thienomorphinans* of the present invention possess *antagonist* activity at the opioid delta receptor in the MVD. They are also of interest as modulatory agents for preventing the development of tolerance and dependence for mu agonist analgesics such as morphine (See page 1, lines 21 to 24 of the specification). Compounds of the present invention are especially useful as analgesics for treating patients suffering from pain (See page 1, lines 18 to 20 of the specification).

Claim 7 is directed to the compound of claim 1 represented by formula II wherein X is  $\text{NH}_2$ , and R is H (See page 5, lines 9 to 11 and page 28, lines 9 and 10 of the specification).

Claim 8 is directed to the compound of claim 1 represented by formula 2 wherein X is  $\text{NH}_2$ , and R is CN (See page 5, lines 9-11; page 13, line 29 to page 14, line 5 of the specification, example 6, compound 8a).



Application No.: 10/049,504

Docket No.: 21381-00053-US

Claim 9 is directed to the compound of claim 1 represented by formula II wherein X is  $\text{NH}_2$ , and R is  $\text{CO}_2\text{R}^2$  (See page 5, lines 9-11; page 14, line 9 to page 15, line 24 of the specification, examples 7, 8 and 9; compounds 8b, 8c and 8d, respectively).

Claim 10 is directed to the compound of claim 1 represented by formula II wherein X is  $\text{NH}_2$ , and R is  $\text{CONH}_2$  (See page 5, lines 9-11; and page 15, line 26 to page 16, line 5 of the specification, example 10, compound 8e).

Claim 11 is directed to the compound of claim 1 represented by formula II wherein X is  $\text{NH}_2$ , and R is  $\text{COC}_6\text{H}_5$  (See page 5, lines 9-11; and page 16, lines 9 to 26 of the specification, example 11, compound 8f).

In addition, biological data is presented for compounds 8a, 8b, 8c, 8d, 8e and 8f in Tables 2 and 3 on pages 21 and 22 of the specification.

#### VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Has the Examiner established that claims 1 and 7-11 are obvious and therefore unpatentable over the cited art and namely over WO96/02545 to Dondio et al.?

#### VII. ARGUMENT

##### A. Dondio et al. Fail to Render Obvious Claims 1 and 7-11

Claims 1 and 7-11 were rejected under 35 U.S.C. §103 (a) as being unpatentable over Dondio et al.

Dondio fails to render obvious claims 1 and 7-11 since, among other things, Dondio does not explicitly disclose the claimed thienomorphinans and the antagonist activity at the opioid delta receptor in the MVD possessed by compounds of this invention.

WO96/02545 specifically discloses only pyrrolomorphinans (pyrrole ring fused to a morphinan unit). Indeed, all of the 19 specifically mentioned compounds are pyrrolomorphinans. Despite this exclusive focus on pyrrole fused morphinans, Dondio alludes to

Application No.: 10/049,504

Docket No.: 21381-00053-US

generic literature methods to synthesize various other heterocycles such as pyridine, pyrazine, thiophene, furan and imidazole (Schemes 3-8).

Eventhough the generic disclosure of Dondio might possibly encompass the compounds of claim 1, because of the vast number of compounds encompassed by Dondio, the claimed compounds are not fairly suggested or rendered obvious. Clearly the preferred compounds of Dondio differ significantly from those of the present invention.

Along these lines, the Board's attention is kindly directed to *In re Baird* 29 USPQ2d 1550 (Fed. Cir. 1994). In *Baird*, the compound recited in the claims (i.e.-bisphenol A) was within the scope of the genus (i.e.-diphenols) disclosed in the prior art. However, just as in the present case, the specific preferred prior art compounds differed from that of the claims. Therefore, because the genus encompassed a large number of possible compounds, analogous to the present case, the Court found that the claims were non-obvious.

Moreover, the primary biological focus of the compounds described in WO 96/02545 relates to the *pyrrolomorphinans* possessing *agonist* activity at the opioid delta receptor (page 8, lines 17-20 in WO 96/02545). Although there is a statement "these compounds displayed also potent delta agonist or antagonist properties in the MVD preparation" (page 11, lines 36-38), the only compound (compound 7) for which pharmacological characterization in the MVD is given shows that this compound is a potent agonist at the receptor (page 12, lines 2-3). In particular, the statement that "(I)n the MVD this compound shows an  $IC_{50}=25nM$  selectively antagonized by 30nM of NTI(10-fold shift of the dose-response curve) demonstrates a potent agonist not antagonist activity at the opioid delta receptor.

In contrast, the present invention describes, for instance, *thienomorphinans* possessing *antagonist* activity at the opioid delta receptor in the MVD (see compounds 8a-8f in Table 3). These compounds are very weak as agonists at the mu receptor in the MVD (0%-15% maximum stimulation at 10  $\mu M$ ) and at the mu receptor in the GPI (0%-40% maximum stimulation at 10  $\mu M$ ). Among compounds 8a-8f, the profile of 8d is that of a mixed antagonist/agonist ligand with high antagonist activity at the delta receptor in the MVD ( $K_e = 5.0 nM$ ) and with no antagonist but modest agonist activity at the mu receptor in the GPI (40% maximum stimulation at 10  $\mu M$ ). Such mixed delta antagonist/mu agonist ligands are of potential interest as analgesic

Application No.: 10/049,504

Docket No.: 21381-00053-US

agents that may be devoid of tolerance and dependence side effects. They are also of interest as modulatory agents for preventing the development of tolerance and dependence for mu agonist analgesics such as morphine. With respect to the pyridomorphinans, please see compounds 7a-7f in Table 3.

Thus the chemical entities (pyrrolomorphinans vs thienomorphinans and pyridomorphinans and the biological activity profile of the compounds described in WO 96/2545(delta agonists) and the present application (delta antagonists) are quite different.

This diametrically opposite activity overcomes the assertion of obviousness stated in the Office Action. Along these lines, see *Ex parte Blattner*, 2 USPQ2d 2047 (BPAI, 1987). In *Blattner*, the invention related to certain azepene compounds having a 7-membered ring as contrasted to the pyrrolidino and piperidino containing 5-and 6 membered "ring homologs" of the prior art. However, analogous to the present case, the claimed compounds possessed utility that was opposite to that of the reference. Accordingly, the Board found that the diametrically opposite utilities overcome an assertion of prima facie obviousness which rises from the expectation that compounds similar in structure will have similar properties. Also see *In re May* 197USPQ601 (CCPA 1978).

The Examiner's reliance on the fact that since compounds according to claim 1 are within the scope of the generic disclosure of Dondio et al., motivation exists to prepare such compounds disregards the well established case law such as *In re Baird*, supra. Patentability of species claims over a disclosed genus are not at all uncommon. This is especially true as in the present case where the activity disclosed and demonstrated for the claimed compounds is diametrically opposite to the activity demonstrated in the cited reference. Furthermore, nothing in the cited reference teaches how the particular compounds shown in examples and tested could be modified to change their properties so drastically as to achieve the opposite activity.

Also, the Examiner's statement that "applicants appear to base their arguments on patentability of the non-elected compounds of formula (I), i.e., pyrrolomorphinans" is in error since our comments as well as the present disclosure at Table 2 and Table 3 disclose opioid receptor binding affinities of the claimed thienomorphinans.

Application No.: 10/049,504

Docket No.: 21381-00053-US

Furthermore, the Examiner's statement that "(A)pplicants do not point to any objective evidence which demonstrates that the claimed compounds as a class exhibit any properties which are actually different from the closest prior compounds embraced by --- " totally disregards the examples and data in the present specification and its comparison to the data shown in Dondio. As discussed previously this data shows the diametrically opposed activity for compounds of the present invention as compared to the tested compound of Dondio. To provide any further comparison would seemingly only repeating what has already been shown. To require more, places an unnecessary burden of time, expense, resources and personnel upon applicant. The reference already provides data on a particular compound, while the present disclosure demonstrates the opposite activity for the claimed compounds. No further evidence is needed since any case of *prima facie* obviousness has been overcome by the present record.

In addition, the case law relied upon by the Examiner does not support the rejection of the claims in view of the difference in the facts in this case as compared to those in the case law relied upon by the Examiner.

For instance in the cases of, *In re Hoch*, *In re Wilder*, *In re Wood* and *In re Payne*, the applicant did not present evidence that was deemed to be of the type needed to rebut a *prima facie* case of obviousness. As mentioned above, compounds of this invention exhibit properties that are the opposite of those of the reference. As discussed above, the present specification contains objective evidence, not merely conclusions, clearly supporting the difference in properties exhibited by the claimed compounds as compared to compounds explicitly tested by Dondio et al. This evidence must be taken into account in evaluating obviousness and cannot be ignored.

On the other hand, *In re Lemin* and *In re Rinehart*, relied upon in a prior Office Action by the Examiner, if anything, support patentability of the present invention. In both of these cases, claims were deemed to be patentable, even though they were within the genus of the prior art.

Furthermore, the cited art lacks the necessary direction or incentive to those of ordinary skill in the art to render a rejection under 35 U.S.C. 103 sustainable. The cited art fails to provide the degree of predictability of success of achieving properties, such as antagonist activity at the opioid delta receptor in the MVD, attainable by the present invention needed to sustain a

Application No.: 10/049,504

Docket No.: 21381-00053-US

rejection under 35 U.S.C. 103. See *Diversitech Corp. v. Century Steps, Inc.* 7 USPQ2d 1315 (Fed. Cir. 1988), *In re Mercier*, 185 USPQ 774 (CCPA 1975) and *In re Naylor*, 152 USPQ 106 (CCPA 1966).

Moreover, properties of the subject matter and improvements which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 U.S.C. 103. See *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d. 1923 (Fed. Cir. 1990), *In re Antonie*, 195, USPQ 6 (CCPA 1977), *In re Estes*, 164 USPQ (CCPA 1970), and *In re Papesch*, 137 USPQ 43 (CCPA 1963).

No property can be ignored in determining patentability and comparing the claimed invention to the cited art. Along these lines, see *In re Papesch*, supra, *In re Burt et al*, 148 USPQ 548 (CCPA 1966), *In re Ward*, 141 USPQ 227 (CCPA 1964, and *In re Cescon*, 177 USPQ 264 (CCPA 1973).

#### B. Additional Argument Concerning the Patentability of Claims 7-11

Furthermore, the generic disclosure of Dondio does not even remotely suggest the compounds of claims 7-11 since Dondio fails to disclose a NH<sub>2</sub> group in the position recited in these claims. Accordingly, claims 7-11 are patentable for this additional reason.

In view of the above, each of the claims on appeal is believed to be in immediate condition for allowance. Accordingly, the Board is respectfully requested to reverse the Examiner and allow claims 1 and 7-11.

### VIII. CLAIMS

A copy of the claims involved in the present appeal is attached hereto as Appendix A. As indicated above, the claims in Appendix A do include the amendments filed by Applicant on April 15, 2003, and do not include the amendment(s) filed on February 23, 2005.

### IX. EVIDENCE

No evidence pursuant to §§ 1.130, 1.131, or 1.132 or entered by or relied upon by the Examiner is being submitted.

Application No.: 10/049,504


Docket No.: 21381-00053-US

X. RELATED PROCEEDINGS

No related proceedings are referenced in II. above, or copies of decisions in related proceedings are not provided, hence no Appendix is included.

Dated: 5-25-05

Respectfully submitted,

By 

Burton A. Amernick

Registration No.: 24,852

CONNOLLY BOVE LODGE & HUTZ LLP

1990 M Street, N.W., Suite 800

Washington, DC 20036-3425

(202) 331-7111

(202) 293-6229 (Fax)

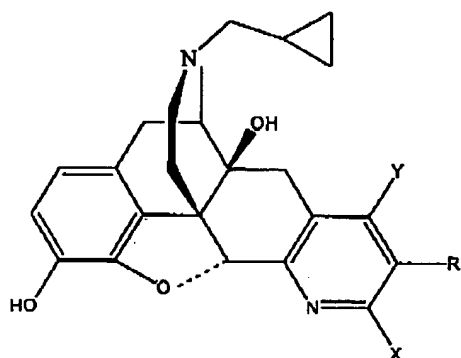
Attorney for Applicant

Application No.: 10/049,504

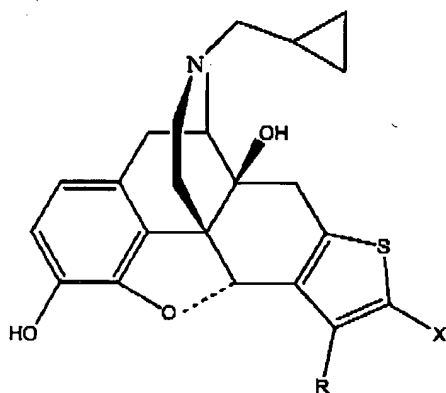
Docket No.: 21381-00053-US

**APPENDIX A****Claims Involved in the Appeal of Application Serial No. 10/049,504**

1. (Previously Presented) A compound represented by the formulae:



I; and



II

Application No.: 10/049,504

Docket No.: 21381-00053-US

wherein each of Y, X and R individually is selected from the group consisting of hydrogen, hydroxyl, halo, CF<sub>3</sub>, NO<sub>2</sub>, CN, NH<sub>2</sub>, COR<sup>1</sup> and CO<sub>2</sub>R<sup>2</sup> wherein R<sup>1</sup> is selected from the group consisting of alkyl, aryl, alkaryl, and NH<sub>2</sub>, and R<sup>2</sup> is selected from the group consisting of alkyl, aryl, and aralkyl, and provided that at least one of Y, X and R in formula I is other than hydrogen; or pharmaceutically acceptable salt thereof.

7. (Original) The compound of claim 1 represented by formula II wherein X is NH<sub>2</sub>, and R is H.

8. (Original) The compound of claim 1 represented by formula 2 wherein X is NH<sub>2</sub>, and R is CN.

9. (Original) The compound of claim 1 represented by formula II wherein X is NH<sub>2</sub>, and R is CO<sub>2</sub>R<sup>2</sup>.

10. (Original) The compound of claim 1 represented by formula II wherein X is NH<sub>2</sub>, and R is CONH<sub>2</sub>.

11. (Original) The compound of claim 1 represented by formula II wherein X is NH<sub>2</sub>, and R is COC<sub>6</sub>H<sub>5</sub>.